

CLAIMS

1. A method for isolating candidate peptides for the treatment of a disease or disorder with a causative agent with SOD activity, the method comprising the steps of:

- 5 (i) contacting a plurality of candidate peptides with a first agent with SOD activity and being causative of the disease or disorder and isolating the bound peptides; and
- (ii) contacting the peptides isolated from step (i) with a second agent structurally related to the first agent but without SOD activity and isolating
- 10 the unbound peptides;

wherein the peptides isolated from step (ii) are candidate peptides for treatment of the disease.

2. A method for isolating candidate peptides for the treatment of a disease or disorder with a causative agent whose SOD activity is dependent on binding copper, the method comprising the steps of:

- (i) contacting a plurality of candidate peptides with a first agent with SOD activity that is adapted to specifically bind copper and isolating the bound peptides; and
- 20 (ii) contacting the peptides isolated from step (i) with a second agent that is structurally related to the first agent but is not adapted to bind copper and isolating the unbound peptides;

wherein the peptides isolated from step (ii) are candidate peptides for treatment of the disease.

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3. A method for isolating candidate peptides for the treatment of a disease or disorder with a causative agent whose toxicity is dependent on binding copper, the method comprising the steps of:

- (i) contacting a plurality of candidate peptides with a first agent that is adapted
- 30 to bind peptides that specifically bind to the copper binding site of the causative agent and isolating the bound peptides; and

(ii) contacting the peptides isolated from step (i) with a second agent that is adapted to bind peptides isolated from step (i) that do not specifically bind to the copper binding site of the causative agent and isolating the unbound peptides;

5 wherein the peptides isolated from step (ii) are candidate peptides for treatment of the disease.

4. A method according to any one of claims 1 to 3 wherein the first and/or second agent is immobilised.

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5. A method according to any one of claims 1 to 3 wherein the first and/or second agent is in solution.

6. A method according to any one of claims 1 to 3 wherein the first and/or
15 second agent further comprises an isolation means that assists in isolating the peptides bound thereto.

7. A method according to any one of claims 1 to 3 wherein the method steps (i) and (ii) are repeated to increase the selectivity of the method.

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8. A method according to claim 7 wherein the amount of the first agent is reduced in each repetition.

9. A method according to claim 8 wherein the amount of the first agent is
25 reduced about 10 fold in each repetition.

10. A method according to claim 7 wherein steps (i) and (ii) are repeated at least 2-3 times.

30 11. A method according to claim 7 wherein the peptides isolated in the first round are amplified to provide a larger quantity for subsequent rounds.

12. A method for isolating candidate peptides for the treatment of AD the method comprising the steps of:

(i) contacting a plurality of candidate peptides with a first agent with SOD activity and isolating the bound peptides; and

5 (ii) contacting the peptides isolated from step (i) with a second agent structurally related to the first agent but without SOD activity and isolating the unbound peptides;

wherein the peptides isolated from step (ii) are candidate peptides for treatment of the disease.

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13. A method according to claim 12 wherein the first agent is A β containing a copper binding site and/or SOD activity or a portion thereof with SOD activity and/or a copper binding site.

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14. A method according to claim 12 or 13 wherein the first agent is human A β .

15. A method according to claim 14 wherein the human A β is human A β ₁₋₄₂ or human A β ₁₋₄₀.

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16. A method according to claim 12 or 13 wherein the first agent is a non-human mammalian A β .

17. A method according to claim 16 wherein the non-human mammalian A β is rabbit, guinea pig, dog, monkey, cow, sheep or polar bear A β .

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18. A method according to claim 12 wherein the second agent is A β that lacks SOD activity and/or a copper binding site or a portion thereof that lacks SOD activity and/or a copper binding site.

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19. A method according to claim 18 wherein the second agent is rat A β .

20. A method according to claim 19 wherein the rat A β is rat A β ₁₋₄₂ or rat A β ₁₋₄₀.

21. A method according to claim 18 wherein the second agent is a non-rat
5 mammalian A β .

22. A method according to claim 21 wherein the non-rat mammalian A β is mouse A β .

10 23. A method for isolating candidate peptides for the treatment of AD, the method comprising the steps of:
(i) contacting a plurality of candidate peptides with a first agent that is adapted to bind peptides that specifically bind to the copper binding site of A β and isolating the bound peptides; and
15 (ii) contacting the peptides isolated from step (i) with a second agent that is adapted to bind peptides isolated from step (i) that do not specifically bind to the copper binding site of A β and isolating the unbound peptides;
wherein the peptides isolated from step (ii) are candidate peptides for AD treatment.

20 24. A method according to any one of claims 1 to 3 wherein the first and second agents are naturally occurring molecules.

25 25. A method according to any one of claims 1 to 3 wherein the first and second agents are non-naturally occurring molecules that have been produced to mimic one or more characteristics of the naturally occurring molecules that are important for the screen.

26. A peptide identified using the method according to any one of claims 1 to 3.

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27. A peptide comprising a sequence selected from the group of sequences:
(i) Met-Thr-Met-Pro-Thr-Met;

(ii) Pro-Leu-Pro-Gln-Met-Leu; and
(iii) Thr-Asn-Pro-Asn-Arg-Arg-Asn-Arg-Thr-Pro-Gln-Met-Leu-Lys-Arg;
or a functional variant thereof.

5 28. A peptide according to claim 26 that binds at or near a copper binding site of A β and physically prevents the binding of copper.

 29. A peptide according to claim 26 wherein the peptide binds at or near amino acids 5-14 of human A β .

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 30. A peptide according to claim 26 wherein the peptide binds at or near amino acids 8-14 of human A β .

 31. A peptide according to 26 wherein the peptide binds at or near amino acid 13 of human A β .

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 32. A peptide according to claim 26 that binds to A β and disrupts the conformation (or 3-D structure) of the copper binding site to reduce or totally remove its ability to bind copper and/or its SOD activity.

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 33. A peptide according to claim 32 that binds and disrupts the conformation of amino acids 5-14 of human A β .

 34. A peptide according to claim 32 that binds and disrupts the conformation of amino acids 8-14 of human A β .

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 35. A peptide according to claim 32 that binds and disrupts the conformation of amino acid 13 of human A β .

30 36. A peptide according to claim 26 that binds to A β and reduces or totally removes its SOD activity whilst still allowing the A β to bind copper.

37. A functional variant of the peptides of claim 26 or 27.
38. A non-peptide peptidomimetic of a peptide according to claim 26 or 27.
- 5 39. A polynucleotide encoding a peptide according to claims 26 or 27.
40. The use of a peptide according to claim 26 or 27 for designing a mimetic thereof.
- 10 41. A method for reducing or removing SOD activity or inhibiting the copper binding ability of a causative agent, the method comprising contacting the causative agent with a peptide identified using the screen of the present invention such that the peptide binds to the causative agent in a fashion that at least reduces its SOD and/or copper binding activity.
- 15 42. A method for destabilizing multimeric forms of A β , the method comprising contacting the multimeric A β with a peptide of the present invention such that the peptide binds to the multimeric A β in a fashion that destabilizes the multimeric A β .
- 20 43. A method for limiting or preventing the aggregation of A β , the method comprising contacting the A β with a peptide of the present invention such that the peptide binds to the A β and prevents or limits its aggregation.
- 25 44. A method of treating a disease or disorder selected from the group comprising type II diabetes, AD, Scrapie and Transmissible Spongiform Encephalopathies such as Creutzfeldt Jacob disease (CJD), variant CJD, Gerstmann Strausler Schinkler syndrome and Bovine Spongiform Encephalopathy (BSE) comprising the step of administering an effective amount of a peptide identified using
- 30 the screening method of the present invention.

45. A pharmaceutical composition comprising a peptide according to claim 26 or 27 and a pharmaceutically acceptable carrier or diluent.

46. A method for isolating candidate peptides for the treatment of AD, the
5 method comprising the steps of:

(i) contacting a plurality of candidate peptides with a first agent that is adapted to bind peptides that specifically bind to the zinc binding site of A β and isolating the bound peptides; and

(ii) contacting the peptides isolated from step (i) with a second agent that is
10 adapted to bind peptides isolated from step (i) that do not specifically bind to the zinc binding site of A β and isolating the unbound peptides;

wherein the peptides isolated from step (ii) are candidate peptides for AD treatment.